FFR 7.8 2008
Under the Paperwork Reductor Act of 1995, no persons are required to re

**FORM** 

(to be used for all correspondence after initial filing)

03-03-08

1635

PTO/SB/21 (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

	• •	
Application Number	10/523,714	
Filing Date	March 28, 2006	
First Named Inventor	Puthupparampil V. Scaria	
Art Unit	1635	
Examiner Name	Louis V. Wollenberger	
Attorney Docket Number	INTM/016	

Total Number of Pages in This Submission	Attorney Docket Number INTM/(	016		
ENCLOSURES (Check all that apply)				
Fee Transmittal Form	Drawing(s)	After Allowance Communication to TC		
Fee Attached  Amendment/Reply  After Final  Affidavits/declaration(s)  Extension of Time Request  Express Abandonment Request	Licensing-related Papers  Petition Petition to Convert to a Provisional Application Power of Attorney, Revocation Change of Correspondence Address Terminal Disclaimer  Request for Refund	Appeal Communication to Board of Appeals and Interferences  Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)  Proprietary Information  Status Letter  Other Enclosure(s) (please Identify below): Form PTO/SB/08a;		
Information Disclosure Statement	CD, Number of CD(s)  Landscape Table on CD	71 Cited References; and Return Receipt Postcard		
Certified Copy of Priority Document(s)  Reply to Missing Parts/ Incomplete Application Reply to Missing Parts under 37 CFR 1.52 or 1.53	Remarks  The Director is hereby authorized to charge payment of any fees required in connection with filing of these papers to Deposit Account No. 06-1075, Order No. 104825-0016. A duplicate copy of this letter is transmitted herewith.			
SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT				
Firm Name Ropes & Gray LLP				
Signature Alle Dec				
Printed name Alla Brukman				
Date February 28, 2007	Reg. No.	61,254		
CERTIFICATE OF EXPRESS MAIL (EXPRESS MAIL LABEL NO. EM014771494US)  I hereby certify that this correspondence is being deposited with the United States Postal Service "EXPRESS MAIL POST OFFICE TO				

Patents, P.O. Box 1450, Alexandria, VA 22373-1450:

Signature

SARAH SCHLIE

Date February 28, 2007

ADDRESSEE" service under 37 C.F.R. §1.10 on the date indicated above and is addressed to Mail Stop; Amendment, Commissioner for

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



# THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Puthupparampil V. Scaria et al.

Application No. : 10/523,714 Confirmation No. : 8393

Filed : March 28, 2006

For : METHODS OF DOWN REGULATING TARGET

GENE EXPRESSION IN VIVO BY INTRODUCTION

OF INTERFERING RNA

Group Art Unit : 1635

Examiner : Louis V. Wollenberger

New York, New York February 28, 2008

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450

## INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.R.F. § § 1.56 and 1.97, applicants hereby make of record the

following documents. Copies of all non-U.S. patent documents are submitted herewith.<sup>1</sup>

<sup>&</sup>lt;sup>1</sup> A completed PTO/SB/08A listing these documents is attached hereto.

Information Disclosure Statement dated February 28, 2008

#### **United States Patents**

Patent No.	<b>Applicant</b>	Issue Date
6,506,559	Fire et al.	01-14-2003
6,657,054	Sun et al.	12-02-2003

## Foreign Patent Publications

Publication No.	<u>Publication Date</u>
WO 99/53050	10-21-1999
WO 01/47496	07-05-2001
WO 01/49324	07-12-2001
WO 01/68836	09-20-2001
WO 01/75164	10-11-2001
WO 02/44321	06-06-2002
WO 03/63765	08-07-2003

#### Non-Patent Literature Documents

AIHARA, H. et al., "Gene transfer into muscle by electroporation in vivo," Nature Biotechnology, 16:867-870 (1998).

BERNSTEIN, E. et al., "Role for a bidentate ribonuclease in the initiation step of RNA interference," Nature, 409:363-366 (2001).

BROWN et al., "RNA Interference in Mammalian Cell Culture: Design, Execution and Analysis of the siRNA Effect," Ambion TechNotes, 9(1):3-5 (2002).

BRUMMELKAMP, T.R. et al., "A System for Stable Expression of Short Interfering RNAs in Mammalian Cells," Science, 296:550-553 (2002).

CAPLEN, N.J. et al., "Specific inhibition of gene expression by small double-stranded RNAs in invertebrate and vertebrate systems," Proc. Natl. Acad. Sci. USA, 98(7):9742-9747.

Application No: 10/523,714

Information Disclosure Statement dated February 28, 2008

CHECK, E, "RNA to the rescue?", Nature, 425:10-12 (2003).

COGONI, C. et al., "Transgene silencing of the al-1 gene in vegetative cells of Neurospora is mediated by a cytoplasmic effector and does not depend on DNA-DNA interactions or DNA methylation," The EMBO Journal, 15(12):3153-3163 (1996).

COGONI, C. et al., "Post-transcriptional gene silencing across kingdoms," Current Opinion in Genetics and Developments, 10:638-643 (2000).

DZITOYEVA, S. et al., "Intra-abdominal injection of double-stranded RNA into anesthetized adult Drosophila triggers RNA interference in the central nervous system," Molecular Psychiatry, 6:665-670 (2001).

ELBASHIR, S.M. et al., "RNA interference is mediated by 21- and 22-nucleotide RNAs," Genes & Development, 15:188-200 (2001).

ELBASHIR, S.M. et al., "Functional anatomy of siRNAs for mediating efficient RNAi in Drosophila melanogaster embryo lysate," The EMBO Journal, 20(23):6877-6888 (2001).

ELBASHIR, S.M. et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," Nature, 411:494-498 (2001).

FIRE, A. et al., "Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans," Nature, 391:806-811 (1998).

GRISHOK, A. et al., "Genetic Requirements for Inheritance of RNAi in C. elegans," Science, 287:2494-2497 (2000).

GRISHOK, A. et al., "Genes and Mechanisms Related to RNA Interference Regulate Expression of the Small Temporal RNAs that Control C. elegans Developmental Timing," Cell, 106:23-34 (2001).

GUO, S. et al., "par-1, a Gene Required for Establishing Polarity in C. elegans Embryos, Encodes a Putative Ser/Thr Kinase That Is Asymmetrically Distributed," Cell, 81:611-620 (1995).

GURA, T., "A silence that speaks volumes," Nature, 404:804-808 (2000).

HAMILTON, A.J. et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants," Science, 286:950-952 (1999).

HAMMOND, S. M. et al., "An RNA-directed nuclease mediates post-transcriptional gene silencing in Drosophila cells," Nature, 404:293-296 (2000).

HAMMOND, S. M. et al., "Post-Transcriptional Gene Silencing By Double-Stranded RNA," Nature Rev. Gen., 2:110-119 (2001).

HOLEN, T. et al., "Positional effects of short interfering RNAs targeting the human coagulation trigger Tissue Factor," Nucleic Acids Research, 30(8):1757-1766 (2002).

HUNTER, C. P., "Gene silencing: Shrinking the black box of RNAi," Current Biology, 10(4):R137-R140 (2000).

HUTVÁGNER, G et al., "A Cellular Function for the RNA-Interference Enzyme Dicer in the Maturation of the let-7 Small Temporal RNA," Science, 293:834-838 (2001).

HUTVÁGNER, G. et al., "RNAi: nature abhors a double-strand," Current Opinion in Genetics & Development, 12:225-232 (2002).

INGELBRECHT, I. et al., "Posttranscriptional silencing of reporter transgenes in tobacco correlates with DNA methylation," Proc. Natl. Acad. Sci. USA, 91:10502-10506 (1994).

JARVIS, R.A. et al., "The siRNA Target Site Is an Important Parameter for Inducing RNAi in Human Cells," Ambion Tech Notes, 8(5) (2001).

JORGENSEN, R. A. et al., "Chalcone synthase cosuppression phenotypes in petunia flowers: comparison of sense vs. antisense constructs and single-copy vs. complex T-DNA," Plant Molecular Biology, 31:957-973 (1996).

KAMATH, R.S. et al., "Effectiveness of specific RNA-mediated interference through ingested double-stranded RNA in Caenorhabditis elegans," Genome Biology, 2(1):2-10 (2000).

KENNERDELL, J. R. et al., "Use of dsRNA-Mediated Genetic Interference to Demonstrate that frizzled and frizzled 2 Act in the Wingless Pathway," Cell, 95:1017-1026 (1998).

KENNERDELL, J. R. et al., "Heritable gene silencing in Drosophila using double-stranded RNA," Nature Biotechnology, 18(8):896-898 (2000).

KETTING, R. F. et al., "mut-7 of C. elegans, Required for Transposon Silencing and RNA Interference, Is a Homolog of Werner Syndrome Helicase and RNaseD," Cell, 99:133-141 (1999).

KETTING, R. F. et al., "Dicer functions in RNA interference and in synthesis of small RNA involved in developmental timing in C. elegans," Genes & Development, 15:2654-2659 (2001).

LAGOS-QUINTANA, M. et al., "Identification of Novel Genes Coding for Small Expressed RNAs," Science, 294:853-858 (2001).

LAU, N. C. et al., "An Abundant Class of Tiny RNAs with Probable Regulatory Roles in Caenorhabditis elegans," Science, 294:858-862 (2001).

LEE et al., "Expression of small interfering RNAs targeted against HIV-1 rev transcripts in human cells," Nature Biotechnology, 19:500-505 (2002).

LEE, R. C. et al., "An Extensive Class of Small RNAs in Caenorhabditis elegans," Science, 294:862-864 (2001).

LIPARDI, C. et al., "RNAi as Random Degradative PCR: siRNA Primers Convert mRNA into dsRNAs that Are Degraded to Generate New siRNAs," Cell, 107:297-307 (2001).

LU, P. Y. et al., "Tumor inhibition by siRNA-Mediated Anti-Angiogenesis in Xenografted Tumor Models," Keystone Symposia, p 219 (2003).

LU, P.Y. et al., "Tumor inhibition By RNAI-Mediated VEGF and VEGFR2 Down Regulation in Xenograft Models," Cancer Gene Therapy, 10:, Supplement 1, 011 (2002).

LU, P.Y. et al., "siRNA-mediated antitumorigenesis for drug target validation and therapeutics," Current Opinion in Molecular Therapeutics, 5(3):225-234 (2003).

MANCHE, L. et al., "Interactions between Double-Stranded RNA Regulators and the Protein Kinase DAI," Molecular and Cellular Biology, 12(11):5238-5248 (1992).

MCCAFFREY, A. et al., "RNA interference in adult mice," Nature, 418:38-39 (2002).

MINKS, M. A. et al., "Structural Requirements of Double-stranded RNA for the Activation of 2',5'-Oligo(A) Polymerase and Protein Kinase of Interferon-treated HeLa Cells," The Journal of Biological Chemistry, 254(20):10180-10183 (1979).

MIYAGISHI, M. et al., "U6 promoter-driven siRNAs with four uridine 3' overhangs efficiently suppress targeted gene expression in mammalian cells," Nature Biotechnology, 19:497-500 (2002).

NAPOLI, C. et al., "Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes in trans," Plant Cell, 2:279-289 (1990).

NOVINA, C. D. et al., "The RNAi revolution," Nature, 430: 161-164 (2004).

NYKÄNEN, A. et al., "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell, 107:309-321 (2001).

PADDISON, P. J. et al., "Short hairpin RNAs (shRNAs) induce sequence-specific silencing in mammalian cells," Genes & Development, 16:948-958 (2002).

PADDISON, P. J. et al., "Stable suppression of gene expression by RNAi in mammalian cells," Proc. Natl. Acad. Sci. USA, 99(3):1443-1448 (2002).

PALAUQUI, Jean-Chrostophe et al., "Systemic acquired silencing: transgene-specific post-transcriptional silencing is transmitted by grafting from silenced stocks to non-silenced scions," The EMBO Journal, 16(15):4738-4745 (1997).

PAUL, C. P. et al., "Effective expression of small interfering RNA in human cells," Nature Biotechnology, 20:505-508 (2002).

RUVKUN, G., "Glimpses of a Tiny RNA World," Science, 294:797-799 (2001).

SCHMID, A. et al., "Combinatorial RNAi: a method for evaluating the functions of gene families in Drosophila," Trends Neurosciences, 25(2):71-74 (2002).

SHARP, P. A. et al., "RNA Interference," Science, 287:2431-2433 (2000).

SHARP, P. A. et al., "RNA interference – 2001," Genes & Development, 15:485-490 (2001).

SUI, G. et al., "A DNA vector-based RNAi technology to suppress gene expression in mammalian cells," Proc. Natl. Acad. Sci. USA, 99(8):5515-5520 (2002).

TABARA, H. et al., "RNAi in C. elegans: Soaking in the Genome Sequence," Science, 282:430-431 (1998).

TIMMONS, L. et al., "Ingestion of bacterially expressed dsRNAs can produce specific and potent genetic interference in Caenorhabditis elegans," Gene, 263: 103-112 (2001).

TIMMONS, L. et al., "Specific interference by ingested dsRNA," Nature, 395:854 (1998).

WIANNY, F. et al., "Specific interference with gene function by double-stranded RNA in early mouse development," Nature Cell Biology, 2:70-75 (2000).

WORBY, C. A. et al., "RNA Interference of Gene Expression (RNAi) in Cultured Drosophila Cells," Science STKE, 95:1-8 (2001).

YANG, S et al., "Specific Double-Stranded RNA Interference in Undifferentiated Mouse Embryonic Stem Cells," Molecular and Cellular Biology, 21(22):7807-7816 (2001).

YU et al., "RNA interference by expression of short-interfering RNAs and hairpin RNAs in mammalian cells," Proc. Natl. Acad. Sci. USA, 99(9):6047-6052 (2002).

ZAMORE, P.D. et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell, 101:25-33 (2000).

## **REMARKS**

Applicants request that the cited documents be (1) fully considered by the Examiner during the course of examination of this application, and (2) printed on any patent issuing from this application. Additionally, applicants request that a copy of Form PTO/SB/08A, as considered and initialed by the Examiner, be returned with the next communication.

This Statement is submitted before the mailing of the first Office Action on the merits. In accordance with 37 C.F.R. § 1.97 (b)(3), no fee is due in connection with this Statement. However, if for any reason a fee is due, the Director is hereby authorized to charge payment of the fee to Deposit Account No. 06-1075, Order No. 104825-0016. A duplicate copy of this Statement is enclosed.

Respectfully submitted,

Jane T. Gunnison (Reg. No. 38,479)

Attorney for Applicants

Alla Brukman (Reg. No. 61,254)

Agent for Applicants

**ROPES & GRAY LLP** 

Customer No. 1473

1211 Avenue of the Americas

New York, New York 10036

Tel.: (212) 596-9000

Fax: (212) 596-9090